

Part I Overview Information

Department of Health and Human Services

Participating Organizations

National Institutes of Health (NIH), (<http://www.nih.gov>)

Components of Participating Organizations

National Institute of Mental Health (NIMH), (<http://www.nimh.nih.gov/>)

National Institute on Aging (NIA), (<http://www.nia.nih.gov/>)

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), (<http://www.niams.nih.gov/>)

National Institute of Biomedical Imaging and Bioengineering (NIBIB), (<http://www.nibib.nih.gov/>)

National Institute on Drug Abuse (NIDA), (<http://www.nida.nih.gov/>)

National Institute of Neurological Disorders and Stroke (NINDS), (<http://www.ninds.nih.gov/>)

Title: Functional Links between the Immune System, Brain Function and Behavior

Announcement Type

This is a reissue of [PA-02-045](#) which was previously released on January 16, 2002

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Key Dates

Release Date: February 14, 2005

Application Receipt Date(s): <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Peer Review Date(s): <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Council Review Date(s): <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Earliest Anticipated Start Date: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Expiration Date: July 2, 2008

Due Dates for E.O. 12372

Not Applicable

Additional Overview Content

Executive Summary

The National Institute of Mental Health (NIMH), National Institute on Aging (NIA), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute on Drug Abuse (NIDA), National Institute of Biomedical Imaging and Bioengineering (NIBIB), and National Institute on Neurological Disorders and Stroke (NINDS) request research grant applications to study neuroimmune molecules and mechanisms involved in regulating normal and pathological central nervous system (CNS) function. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. The total amount awarded and the number of awards will depend upon the mechanism numbers, quality, duration, and costs of the applications received. This PA will use the NIH R01, R21, and R03 award mechanisms. Applications may be submitted by domestic or foreign, for-profit or non-profit organizations, public or private institutions, such as universities, colleges, hospitals, and laboratories; units of State and local governments; eligible agencies of the Federal government. Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs. There is no limit on the number of applications that may be submitted. Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

Background

Despite the brain's status as an immune privileged site, an extensive bi-directional communication takes place between the nervous and the immune system in both health and disease. Immune cells and neuroimmune molecules such as cytokines, chemokines, and growth factors modulate brain function through multiple signaling pathways throughout the lifespan. Immunological, physiological and psychological stressors engage cytokines and other immune molecules as mediators of interactions with neuroendocrine, neuropeptide, and neurotransmitter systems. For example, brain cytokine levels increase following stress exposure, while treatments designed to alleviate stress reverse this effect.

Neuroinflammation and neuroimmune activation have been shown to play a role in the etiology of a variety of neurological disorders such as stroke, Parkinson's and Alzheimer's disease, multiple sclerosis, pain, and AIDS-associated dementia. However, cytokines and chemokines also modulate CNS function in the absence of overt immunological, physiological, or psychological challenges. For example, cytokines and cytokine receptor inhibitors affect cognitive and emotional processes. Recent evidence suggests that immune molecules modulate brain systems differently across the lifespan. Cytokines and chemokines regulate neurotrophins and other molecules critical to neurodevelopmental processes, and exposure to certain neuroimmune challenges early in life affects brain development. In adults, cytokines and chemokines affect synaptic plasticity and other ongoing neural processes, which may change in aging brains. Finally, interactions of immune molecules with the hypothalamic-pituitary-gonadal system indicate that sex differences are a significant factor determining the impact of neuroimmune influences on brain function and behavior.

Research Scope

The potent effects of neuroimmune molecules in the brain are mediated through multiple signaling pathways. However, details regarding the extent, routes, or mechanisms whereby immune signaling affects the brain in either normal conditions or during immune challenge and inflammation are largely unexplored. The purpose of this PA is to identify research opportunities that may help to bridge the gap in understanding how immune cells and their mediators affect brain development, function and behaviors related to cognition and mood. This includes studies of the effects of immune molecules and cells on molecular and cellular neural processes, neuronal signaling, glial-neural interactions, neural activation, and objective behavioral endpoints of relevance to mood, cognition, and motivation. Studies examining immune effects on neurodevelopment and across the lifespan as well as studies comparing effects in males and females are also encouraged.

It should be noted that studies aimed at examining how the brain or stressors affect peripheral immune function are not appropriate for this solicitation. Similarly, studies of immune cell entry and fate in brain are appropriate only if they examine how these cells affect ongoing brain processes and/or behavior.

Examples of Areas of interest include, but are not limited to:

Characterization of pathways that mediate the effects of peripheral and central immune activation on brain across the lifespan:

- Identify and characterize relevant brain receptors and signal transduction mechanisms.
- Identify factors regulating brain cytokine and chemokine expression, release, inactivation and degradation during development and throughout the lifespan.
- Determine the role of neurotransmitters, neuropeptides, and neurohormones as potential mediators and/or modulators of cytokine and chemokines expression and signaling in brain.
- Examine effects of cytokines and chemokines on gene expression and activation of neurotransmitters, neurohormones, and other signaling molecules in brain.
- Examine the role of immune cells and molecules in neural-glial communication.
- Examine the developmental expression of cytokines, chemokines, receptors, and related signaling molecules in brain.
- Examine the neurobiological impact of developmental changes in blood brain barrier function and immune molecule infiltration of brain.
- Determine the effects of immune molecules on brain stem cell production and fate.
- Examine the role of acute and chronic infection on brain function and behavior throughout the lifespan.
- Examine interactions of cytokines and chemokines with acute and chronic psychoactive drugs in brain at molecular, cellular, and behavioral levels.

Physiological and behavioral actions of immune cells and molecules:

- Examine the impact of immune cells and molecules in well-characterized cellular and behavioral model systems. Examples of areas of study might include neural plasticity, circadian activity, sleep, arousal, pain perception, learning, memory, anxiety or fearfulness, affect, sensory gating, or maternal behavior.
- Examine the mechanisms and outcomes of interactions of immune molecules with acute and chronic psychoactive drugs.
- Examine the long-term consequences of acute and chronic infection throughout the lifespan on susceptibility to adverse

neurophysiological and behavioral effects of stress.

- o Identify anatomical and molecular pathways mediating specific behavioral effects of cytokines, chemokines and other immune mediators.

Development and refinement of animal models of immune signaling in brain:

- Develop and refine models to examine the potential effects of pre- and post-natal infection on brain development and adult brain function and behavior.
- Model chronic therapeutic administration of cytokines as used in chemotherapy to examine the mechanisms responsible for effects on mood and cognition.
- Model effects of acute and chronic immune challenge on neuroendocrine systems, neurochemistry, electrophysiology, molecular signaling, and gene expression in neurons and glia.
- Model neural effects of autoreactive T and B cells and immune molecules implicated in autoimmune disorders affecting neurophysiological function and mental health.
- Examine the role of the blood brain barrier in neuroimmune responses.

Development and refinement of research tools to examine how immune molecules affect brain function and behavior:

- Develop and characterize cytokine and chemokine receptor selective ligands.
- Develop neuroimaging tools to study immune effects within specific brain regions.
- Develop tools for examining blood/brain barrier permeability to immune molecules, cells, and antibodies.
- Develop biomarkers to assess neurobiological impact of current or previous immune activation in the brain.
- Develop genetic tools to alter selective components of the immune system and brain signaling pathways within limited developmental periods.

Genetic determinants of immune responses in brain:

- Model and examine genetic variations of immune molecule expression as potential susceptibility factors for developing neuropsychiatric symptoms.
- Examine combined effects of stress and/or adverse early environmental experience with genetic alterations in immune signaling in predisposing patterns of brain development and behavior.
- Examine the impact of genetic manipulation of cytokines/chemokines and their receptors, neurotransmitters, peptides, receptors, hormones, or other signaling molecules on brain signaling and behavior.

Clinical applications:

- Employ functional imaging in basic and clinical studies to determine the effects of immune molecules and cells, infection, and autoimmune-responses on brain function.
- Enhance translational efforts to identify cellular and molecular mediators of neuropsychiatric symptoms associated with naturally occurring conditions of immune compromise or cytokine therapy.
- Identify biomarkers of CNS impact of infection and autoimmune disorders.
- Develop non-invasive methods to assess blood brain barrier integrity in clinical populations.
- Explore CNS and behavioral consequences of comorbidity of immune system deregulation with mental disorders.
- Identify and characterize autoantibodies and their target molecules in animal models and in neuropathological studies using clinical brain and CSF samples from Sydenham's Chorea patients and from other psychiatric populations of suspected autoimmune origin.

The NIAMS encourages applications to study immune-CNS interactions in rheumatic diseases. Rheumatic diseases such as systemic lupus erythematosus (SLE) and rheumatic arthritis (RA) are autoimmune diseases whose clinical manifestation often include intermittent or progressive neuropsychiatric dysfunction, including depression, memory loss, concentration deficits, dementia, and anxiety syndromes. In general, a fluctuating course of disease rather than a rapid decline to dementia is characteristic. Cognitive impairment can occur in isolation or in the context of other neurologic or psychiatric syndromes such as depression or psychosis. Certain deficits are specifically associated with particular serum autoantibodies. For example, recent reports have shown lupus psychosis to be associated with the presence of antibodies directed against the carboxyl terminus of the ribosomal P proteins, and a shared amino acid sequence between HLA-DQB1 and P peptides was strongly associated with anti-P antibodies in SLE, suggesting the presence of autoreactive T cells directed against P proteins. The mechanisms explaining these associations and their contribution to disease pathogenesis are uncertain. Research in these areas could improve significantly with the development of new techniques and with the development of new animal models to explore the pathogenesis of cognitive and psychiatric disorders in the rheumatic diseases.

Examples of areas of NIAMS interest include, but are not limited to:

- Studies designed to discover the links between immune dysfunction and nervous system involvement in RA, SLE, scleroderma,

and other rheumatic diseases, including studies in new and existing animal models of disease.

- Hypothesis-generating studies of murine and human neuropsychiatric SLE to examine the role of inflammatory mediators and inflammation of the central nervous system and/or its vasculature in NP-SLE pathophysiology, e.g., endothelial activation, immune complex deposition and effacement of the blood-brain barrier, pericyte and microglial activation, abnormalities in neurotransmission and neurophysiology, autoantibodies such as antiphospholipid antibodies, etc.
- Assessment of structural and functional aspects of the nervous system in rheumatic diseases (i.e., by neuroimaging or neuropathology).
- Evaluation of prospective biomarkers of CNS involvement in rheumatic disease, including biological, imaging, and other modalities that reflect normal or abnormal neuro-immune processes.
- Neurobehavioral evaluation of murine models of SLE.
- Evaluation of neurobehavioral effects secondary to treatment of rheumatic disease.

The NIBIB solicits applications towards the:

- Development, improvement, and novel application of imaging and image analysis tools for studies of the impact of immune molecules in neural plasticity, brain development, and brain function.
- Study of immune – CNS interactions through the development and advancement of imaging and image analysis

Section II. Award Information

1. Mechanism(s) of Support

This PA will use the National Institutes of Health (NIH) research project grant (R01), Small Grant (R03), and Exploratory/Developmental grant (R21) (see <http://grants.nih.gov/grants/funding/r21.htm>) award mechanisms. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. This funding opportunity uses just-in-time concepts. It also uses the modular as well as the non-modular budget formats (see <http://grants.nih.gov/grants/funding/modular/modular.htm>). Specifically, if you are submitting an application with direct costs in each year of \$250,000 or less, use the modular budget format described in the PHS 398 application instructions. Otherwise follow the instructions for non-modular research grant applications.

2. Funds Available

Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of the IC(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications. Fiscal and administrative costs are not included in the direct cost limitation, see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-004.html>.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristics:

- For-profit organizations
- Non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State government
- Units of local government
- Eligible agencies of the Federal government
- Foreign Institutions
- Domestic Institutions
- Faith-based or community-based organizations

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their

institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

2. Cost Sharing or Matching

Not applicable

3. Other-Special Eligibility Criteria

This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing.

Section IV. Application and Submission Information

1. Address to Request Application Information

The PHS 398 application instructions are available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at <http://www.dnb.com/us/>. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates and Times

Applications must be mailed on or before the receipt date described at <http://grants.nih.gov/grants/funding/submissionschedule.htm>. Submission times N/A.

3.A. Receipt, Review and Anticipated Start Dates

Application Receipt Dates: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Peer Review Date: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Council Review Date: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

Earliest Anticipated Start Date: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

3.A.1. Letter of Intent

A letter of intent is not required for the funding opportunity.

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

3.C. Application Processing

Applications must be sent on or before the application receipt dates described above ([Section IV.3.A.](#)) and at <http://grants.nih.gov/grants/dates.htm>. Applications will be evaluated for completeness by CSR.

The NIH will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The NIH will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

4. Intergovernmental Review

This initiative is not subject to [intergovernmental review](#).

5. Funding Restrictions

All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm> (see also [Section VI.3. Reporting](#)).

6. Other Submission Requirements

All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm> (See also [Section VI.3. Reporting](#))

Specific Instructions for Modular Grant applications.

Applications requesting up to \$250,000 per year in direct costs must be submitted in a modular budget format. The modular budget format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in \$25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at <http://grants.nih.gov/grants/funding/phs398/phs398.html> includes step-by-step guidance for preparing modular budgets. Additional information on modular budgets is available at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

Specific Instructions for Applications Requesting \$500,000 (direct costs) or More per Year.

Applicants requesting \$500,000 or more in direct costs for any year must carry out the following steps:

- 1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as you are developing plans for the study;
- 2) Obtain agreement from the IC staff that the IC will accept your application for consideration for award; and,
- 3) Include a cover letter with the application that identifies the staff member and IC who agreed to accept assignment of the application.

This policy applies to all investigator-initiated new (type 1), competing continuation (type 2), competing supplement, or any amended or revised version of these grant application types. Additional information on this policy is available in the NIH Guide for Grants and Contracts, October 19, 2001 at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html>.

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

Applicants requesting more than \$500,000 in direct costs in any year of the proposed research must include a plan for sharing research data in their application. The funding organization will be responsible for monitoring the data sharing policy (http://grants.nih.gov/grants/policy/data_sharing).

The reasonableness of the data sharing plan or the rationale for not sharing research data may be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score.

Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (NIH Grants Policy Statement)

http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131). Investigators responding to this funding opportunity should include a plan for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan and any related data sharing plans will be considered by Program staff of the funding organization when making recommendations about funding applications. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590, <http://grants.nih.gov/grants/funding/2590/2590.htm>). See [Section VI.3. Reporting](#).

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process.

2. Review and Selection Process

Applications submitted for this funding opportunity will be assigned to the ICs on the basis of established PHS referral guidelines.

Appropriate scientific review groups convened in accordance with the standard NIH peer review procedures (<http://www.csr.nih.gov/refrev.htm>) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique
- Receive a second level of review by the appropriate national advisory council or board

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

The goals of NIH supported research are to advance our understanding of biological systems, to improve the control of disease, and to enhance health. In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

1. Significance. Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

2. Approach. Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

3. Innovation. Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

4. Investigators. Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

5. Environment. Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

2.A. Additional Review Criteria:

In addition to the above criteria, the following items will continue to be considered in the determination of scientific merit and the priority score:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated (see the Research Plan, Section E on Human Subjects in the PHS Form 398).

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section F of the PHS Form 398 research grant application instructions will be assessed.

2.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research. The priority score should not be affected by the evaluation of the budget.

2.C. Sharing Research Data

Data Sharing Plan: The reasonableness of the data sharing plan or the rationale for not sharing research data may be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The funding organization will be responsible for monitoring the data sharing policy. http://grants.nih.gov/grants/policy/data_sharing.

2.D. Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication (See the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps/part_ii_5.htm#availofrr and http://ott.od.nih.gov/newpages/rtguide_final.html). Investigators responding to this funding opportunity should include a sharing research resources plan addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing plan will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing plans with the awardee before recommending funding of an application. The final version of the data and resource sharing plans negotiated by both will become a condition of the award of the grant. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report (PHS 2590). See [Section VI.3. Reporting](#).

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a Summary Statement.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm).

A formal notification in the form of a Notice of Grant Award (NGA) will be provided to the applicant organization. The NGA signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

The NGA will be sent via email to the administrative official whose name is listed in Block 12 on the Face Page of the Form PHS 398.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm) and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm).

2.A. Cooperative Agreement Terms and Conditions of Award

Not applicable

3. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually (<http://grants.nih.gov/grants/funding/2590/2590.htm>) and financial statements as required in the NIH Grants Policy Statement.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into two areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

Lois Winsky, Ph.D.
Division of Neuroscience and Basic Behavioral Science
National Institute of Mental Health
6001 Executive Boulevard, Room, 7184, MSC 9641
Bethesda, MD 20892-9641
Telephone: (301) 443-5288
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Email: lwinsky@mail.nih.gov

Andrew A. Monjan, Ph.D.
Chief, Neurobiology of Aging Branch
Neuroscience and Neuropsychology of Aging
National Institute on Aging
Gateway Building, Room 350
Bethesda, MD 20892
Telephone: (301) 496-9350
FAX: (301) 402-4740
Email: am39m@nih.gov

Deborah N. Ader, Ph.D.
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National Institute of Arthritis and Musculoskeletal and Skin Diseases
6701 Democracy Blvd., Suite 800
Bethesda, MD 20892
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Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:

Recipients of PHS support for activated involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (<http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf>) as mandated by the Health Research Extension Act of 1985 (<http://grants.nih.gov/grants/olaw/references/hrea1985.htm>), and the USDA Animal Welfare Regulations (<http://www.nal.usda.gov/awic/legislat/usdaleg1.htm>) as applicable.

Human Subjects Protection:

Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>).

Data and Safety Monitoring Plan:

Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity and dose-finding studies (phase I); efficacy studies (Phase II); efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, <http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

Sharing Research Data:

Investigators submitting an NIH application seeking \$500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible (http://grants.nih.gov/grants/policy/data_sharing).

Investigators should seek guidance from their institutions, on issues related to institutional policies and local IRB rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Sharing of Model Organisms:

NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh Dole Act (see the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or contract proposal, beginning with the October 1, 2004 receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Inclusion of Women And Minorities in Clinical Research:

It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research" (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Inclusion of Children as Participants in Clinical Research:

The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects (<http://grants.nih.gov/grants/funding/children/children.htm>).

Required Education on the Protection of Human Subject Participants:

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>.

Human Embryonic Stem Cells (hESC):

Criteria for federal funding of research on hESCs can be found at <http://stemcells.nih.gov/index.asp> and at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html>. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (<http://escr.nih.gov/>). It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s) to be used in the proposed research. Applications that do not provide this information will be returned without review.

Public Access to Research Data through the Freedom of Information Act:

The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Standards for Privacy of Individually Identifiable Health Information:

The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (<http://www.hhs.gov/ocr/>) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html>.

URLs in NIH Grant Applications or Appendices:

All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Healthy People 2010:

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.healthypeople.gov/>.

Authority and Regulations:

This program is described in the Catalog of Federal Domestic Assistance at <http://www.cfda.gov/> and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at <http://grants.nih.gov/grants/policy/policy.htm>.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Loan Repayment Programs:

NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The LRP is an important component of NIH's efforts to recruit and retain the next generation of researchers by providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and

LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40 hour week) for two years to the research. For further information, please see: <http://www.lrp.nih.gov/>.

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